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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/381,497	02/17/2000	DAVID J. FITZGERALD	015280-317100US	4036

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EXAMINER

HELMS, LARRY RONALD

ART UNIT

PAPER NUMBER

1642

DATE MAILED: 04/28/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/381,497

Applicant(s)

FITZGERALD

Examiner

Larry R. Helms

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 23 February 2004.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-4, 7-11, 13, 14, 16, 17, 22-26 and 29-32 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-4, 7-11, 13, 14, 16, 17, 22-26 and 29-32 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

1. Claims 1 and 11 have been amended.

Claims 1-4, 7-11, 13-14, 16-17, 22-26, 29-32 are under examination.

2. The text of those sections of title 35, USC Code not included on the Office Action can be found in a prior Office Action.

Rejections Withdrawn

3. The rejection of claims 11, 13-14, 17 under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention is withdrawn in view of the amendments to the claims.

Response to Arguments

4. The rejection of claims 1-4, 7-11, 13-14, 16-17, 22-26, 29-32 under 35 U.S.C. 103(a) as being unpatentable over Ghetie et al (Cancer Res. 51:5876-5880, 1991) and further in view of Shen et al (Int. J. Cancer 42:792-797, 1988) and Reiter et al (Biochemistry 33:5451-5459, 1994) and Kuan et al (Biochemistry 35:2872-2877, 1996, Abstract published 2/1/96) and Orlandi et al (Proc. Natl. Acad. Sci. USA, 86:3833-3837, 1989), Cabilly et al (U.S Patent 4816567, issued 3/89), Boss et al (U.S Patent 4816397, issued 3/89), Robinson et al (U.S. Patent 5618920, filed 4/94), Ward et al (Nature

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341:544-546, 1989), and Huston et al (U.S. Patent 5258498, issued 11/93) is maintained.

The response filed 2/23/04 has been carefully considered but is deemed not to be persuasive. The response states that the methods are general methods for determining the sequences of variable chain regions and there is no evidence that the prior art would have suggested making specific molecular modifications to achieve the claimed invention (see page 5 of response) and the conjugate RFB4dsFv-PE38 has binding affinity that is essentially equivalent to the unconjugated IgG and that Reiter et al (Nature Biotechnology) show that affinity only equals the IgG only in a majority of cases and RFB4 variable regions have superior expression and a declaration will be prepared to provide further evidence of surprising binding properties (see page 6 of response). In response to these arguments, no declaration has been supplied. In addition, the art demonstrates that the sequence of the variable regions of antibodies are routinely obtained, therefore it would have been obvious to obtain such sequences. In addition, Reiter et al (Nature Biotech) teach 4 out of 8 dsFv-immunotoxins had improved binding affinity (see page 1243, left column). The Reiter et al (Biochemistry) clearly shows better cytotoxicity for the dsFV as compared to the scFv and better expression yields (see Table 1) and better stability (see Table 2) and teach "that dsFv's have at least the same binding properties as scFv's, and in some cases they may be better" (see abstract) and Reiter et al teach that scFv can retain the specificity and affinity of IgG (see page 5451). The Reiter et al (Biochemistry) clearly shows better cytotoxicity for the dsFV as compared to the scFv and better expression yields (see

Table 1) and better stability (see Table 2) and teach "that dsFv's have at least the same binding properties as scFv's, and in some cases they may be better" (see abstract) and Reiter et al teach that scFv can retain the specificity and affinity of IgG (see page 5451). With regard to the Krietman et al reference, this reference demonstrates only one instant where the dsFv had low activity, however, in all of Reiter et al (Biochemistry) and Kuan et al (Biochemistry) the dsFv were active and potent and as such one skill in the art would have a reasonable expectation of success in making the claimed immunoconjugate dsFv with the RFB4 antibody.

Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references.

Conclusions

5. No Claims are allowed.
6. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any

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extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.


7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Larry R. Helms, Ph.D, whose telephone number is (571) 272-0832. The examiner can normally be reached on Monday through Friday from 7:00 am to 4:30 pm, with alternate Fridays off. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler, can be reached at (571) 272-0871.

8. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The Fax Center telephone number is 703-872-9306.

Respectfully,

Larry R. Helms Ph.D.

571-272-0832



LARRY R. HELMS, PH.D
PRIMARY EXAMINER